

What is claimed is:

See B1 1. A method for *in vivo* delivery of a desired composition into human or animal central nervous system (CNS) or spinal cord, wherein the method comprises administering to the human or animal a composition comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) in association with at least a molecule having a biological function and said composition is capable of *in vivo* retrograde axonal transport and transynaptic transport into the CNS or the spinal cord of the human or animal and of being delivered at different areas of the CNS or the spinal cord.

2. The method according to claim 1, wherein the composition is administered into a muscle.

3. The method according to claim 2, wherein the composition is administered into a muscle in the vicinity of a neuromuscular junction.

4. The method according to claim 2, wherein the muscle is selected in relation with the desired area of the CNS or spinal cord.

See C3 5. The method according to claim 1, wherein the composition is administered into neuronal cells.

See B2 6. The method according to claim 1, wherein the composition comprises a non-toxic, proteolytic fragment of tetanus toxin (TT) comprising a fragment C and a fragment B or a fraction thereof of at least 11 amino acid residues in association with at least a molecule having a biological function selected from the group consisting of a protein for compensation or modulation of functions under the control of the CNS or the spinal cord or modulation of functions in the CNS or the

spinal cord or a protein to be delivered by gene therapy expression system to the CNS or the spinal cord.

Sub B2

7. The method according to claim 1, wherein the composition comprises a non-toxic, proteolytic fragment of tetanus toxin (TT) comprising a fragment C and a fragment B or a fraction thereof of at least 11 amino acid residues and a fraction of a fragment A devoid of its toxic activity corresponding to the proteolytic domain having a zinc-binding motif located in the central part of the chain between amino acids 225 and 245 in association with at least a molecule having a biological function selected from the group consisting of protein for the compensation or the modulation of functions under the control of the CNS or the spinal cord or protein to be delivered by gene therapy expression system to the CNS or the spinal cord.

Sub C1

8. The method according to claim 6 or claim 7, wherein the molecule is selected from the group consisting of protein SM, BDNF (Brain-derived neurotrophic factor), NT-3 (Neurotrophin-3), NT-4/5, GDNF (Glial cell-line-derived neurotrophic factor), IGF (Insulin-like growth factor), PNI (protease nexin I), SPI3 (Serine Protease Inhibitor protein), ICE (Interleukin-1 converting enzyme), Bcl-2, GFP (green fluorescent protein), endonucleases like I-SceI or CRE, antibodies, or drugs specifically directed against neurodegenerative diseases such as latero spinal amyotrophy (LSA).

9. The method according to claim 8, wherein the composition comprises a combination of at least two of said molecules.

Sub 8C
10. The method according to claim 8, wherein the molecule is located upstream from the fragment of tetanus toxin.

11. The method according to claim 8, wherein the molecule is located downstream from the fragment of tetanus toxin.

12. The method according to claim 1, which comprises administering to the human or animal a vector containing nucleotides encoding the composition, wherein the vector is capable of *in vivo* expression in a muscle and this product is capable of migrating to the CNS or spinal cord.

13. The method according to claim 12, wherein said vector comprises a promoter and an enhancer capable of expressing the nucleotides contained in said vector in the muscle.

14. The method according to claim 13, wherein said vector is the plasmid pCMV-LacZ-TTC which has been deposited at the C.N.C.M. on August 12, 1997, under the registration number I-1912.

15. The method according to claim 12 or 13, wherein said vector is administered into the muscle.

16. The method according to claim 12 or 13, wherein the molecule is a nucleotide encoding for a protein or a polypeptide linked chemically to the fragment of tetanus toxin and being transported and expressed directly in neurons.

17. A hybrid fragment of tetanus toxin comprising a fragment C and a fragment B or a fraction thereof of at least 11 amino acid residues capable of transferring *in vivo* a protein, a peptide, or a polynucleotide through a neuromuscular junction and at least one synapse.

18. A hybrid fragment of tetanus toxin comprising a fragment C and a fragment B or a fraction thereof of at least 11 amino acid residues and a fraction of a fragment A devoid of its toxic activity corresponding to the proteolytic domain having a zinc-binding motif located in the central part of the chain between amino acids 225 and 245 capable of transferring *in vivo* a protein, a peptide or a polynucleotide through a neuromuscular junction and at least one synapse.

19. An amino acid variant fragment having the same properties as the hybrid fragment of tetanus toxin according to claims 17 or 18.

20. A polynucleotide variant fragment encoding an amino acid variant fragment according to claim 19, which is capable of hybridization under stringent conditions with the natural tetanus toxin sequence.

21. A composition containing an active molecule in association with a hybrid fragment of tetanus toxin according to claims 17 or 18 or with an amino acid variant fragment according to claim 16.

22. The composition according to claim 21, wherein the active molecule is selected from the group consisting of protein SMN, BDNF (Brain-derived neurotrophic factor), NT-3, NT-4/5, GDNF (Glial cell-line derived neurotrophic factor), IGF (Insulin-like

growth factor), PNI (protease nexin I), SP13 (Serine Protease Inhibitor protein), ICE, Bcl-2, GFP (green fluorescent protein), endonucleases like I-SceI or CRE, antibodies or drugs specifically directed against neurodegenerative diseases such as latero spinal amyotrophy (LSA).

23. The composition according to claim 21, wherein the active molecule is a polynucleotide encoding a protein or a polypeptide with a promoter capable of expression in neurons, and optionally an enhancer.

24. A vector comprising a promoter capable of expression in muscle cells and optionally an enhancer, a nucleic acid sequence coding for the fragment of tetanus toxin according to claims 17 or 18 or with an amino acid variant fragment according to claim 19 associated with a polynucleotide coding for a protein or a polypeptide.

25. A cell or vector comprising a promoter capable of expression in neuronal cells or precursors of neuronal cells and optionally an enhancer, a nucleic acid sequence coding for the fragment of tetanus toxin according to claims 17 or 18 or for an amino acid variant fragment according to claim 19, associated with a polynucleotide coding for a protein or a polypeptide.

26. A composition for the treatment of a patient or an animal affected with CNS or spinal cord disease, which comprises delivering a composition according to claims 21, 22, or 23 to the patient or animal in an amount effective for treatment of the CNS or spinal cord disease.

27. A composition for the treatment of a patient or an animal affected with CNS or spinal cord disease, which comprises delivering a vector according to claim 24 or a cell according to claim 25 to the patient or animal in an amount effective for treatment of the CNS or spinal cord disease.

28. The method according to claim 1, which comprises administering to the human or animal a cell or a vector containing nucleotides encoding the composition, wherein the cell or vector is capable of in vivo expression in neuronal cells or precursor of neuronal cells and wherein said cell is reimplanted into the CNS or spinal cord.

29. The method according to claim 28 wherein said cell or vector comprises a promoter and an enhancer capable of expressing the nucleotides contained in said cell in neuronal cells or precursors of neuronal cells.

30. The method according to claim 28 or 29 wherein the molecule is a polynucleotide encoding for a protein or a polypeptide linked chemically to the fragment of tetanus toxin and being expressed directly in neurons.

Sub B3 31. Use of a hybrid fragment of tetanus toxin according to claim 18 or 19 or of a polynucleotide fragment according to claim 20, or a composition according to anyone of claims 21 to 23, or a vector according to claim 24, for the preparation of a composition for the treatment of the CNS or spiral cord disease.